Confirmation of election of Group I.

Applicant hereby confirms the election of Group I made be telephone. Group I features nucleic acids (Claim 1, now canceled, and claims 8-10).

Oath

A new oath is enclosed.

Section 112, paragraph 1

Claim 8 is drawn to a specific cDNA (clone TR2B) which has been deposited with the American Type Culture Collection. Claim 9 is drawn to nucleic acid that hybridizes with TR2B under stringent conditions and enhances a neuroregenerative process. Claim 10 is drawn to fragments of clone TR2B that enhance a neuroregenerative process.

The rejection under section 112 paragraph 1 stems from certain problems the examiner has raised in connection with the deposit of the claimed cDNA. With respect to claim 8, those problems have been corrected by an additional deposit as described below in part I. The examiner's attention to this matter is appreciated. There are no other rejections relevant to claim 8.

The examiner has also raised issues that relate specifically to coverage of fragments and DNA that hybridize to the claimed cDNA, as featured in claims 9 and 10. Those issues are addressed in Part II, below.

I. *CLAIM 8: The problems the examiner cites with the deposits have been corrected by a new deposit.*

The examiner acknowledges that applicant has deposited the claimed clone, but he finds the deposit inadequate to enable the invention. On this point, the examiner says (paper 6, p.5, line 18 through page 6, line 3),

> "Even if ATCC Deposit 68975 was obtained by the skilled artisan, which contains the 500bp sequence, the specification does not describe the vector or cell that the 500bp sequence is present in. One would be required to sequence the whole vector and then determine which 500bp sequence would be the novel insert. The skilled artisan would not be able to make the claimed inventions because no information is disclosed concerning the vectors that the two clones, 68075_{DNA} and TR2B, are contained in the cells identified as ATCC 68075 and 75949, respectively."

Actually, the specification does disclose that the clones were obtained in λGT11 vectors. See the specification at page 8, lines 1-33:

> "...double-stranded cDNA was treated with *Eco*R1, ... The cDNA was ligated to lambda gt11 DNA.... Approximately 500ng of cDNA was ligated to 50ng of lambda gt11 arms.... The DNA was packaged according to standard protocols and amplified in *E. coli* ....
>
> A preliminary screening of the library using [certain anti-idiotype antibodies] revealed a single positive clone ... now called 68075_{DNA}.
>
> Rescreening of the brain library with the [above positive clone] identified .... clones [including TR2B] to which the 500 base clone hybridized.

In short, the art reading the specification would have no doubt that the clones obtained by rescreening (of which TR2B was one) were present in a lambda gt11 vector. It is not accurate to say that the specification does not describe the vector that contained the claimed cDNA.

The examiner has identified a problem, however, in that the deposits actually were made in the form of *E. Coli* cells containing the cDNA on a plasmid. The examiner has correctly indicated that the plasmid is not referenced in the specification. Rather than take issue on the question of whether the art could obtain the claimed cDNA from the deposited plasmid, applicant has made an additional deposit of the TR2B cDNA in the λGT11 vector -- i.e., the vector referenced in the specification. The form accompanying that deposit is enclosure A to this Amendment. When applicant receives confirmation of the accession number assigned to that deposit, the claims will be amended to recite that number.

One skilled in the art would now have the requisite information to retrieve the claimed cDNA. Specifically, based on the disclosure in the specification that the cDNA is present in a λGT11 vector, the art would have all of the information necessary to retrieve that cDNA. The examiner specifically mentions the need to know which restriction sites the vector contains. Since well before applicant's filing date, the art has been well aware of λGT11, a widely used commercial vector having a specific unique *Eco*R1 cloning site. Not only was λGT11 widely available, it had been well characterized. Just one example of a readily available characterization of λgt11 is the 1987/1988 Promega Biological Research Products Catalogue and Reference Guide. That Guide says,

> "Lambda gt11 is a cloning and expression vector [citing Young and Davis, *Proc. Natl. Acad. Sci. USA*, 80:1194-1198

(1983)] used in constructing cDNA and genomic libraries. The *Eco*R1 insertion site is located within the *lac*Z gene, upstream from the β-galactosidase translation termination codon."

The catalogue also includes a map of the key features of λgt11, including the unique *Eco*R1 site. There is no question that the art would know exactly how to retrieve the claimed cDNA from the material now on deposit with the ATCC, by digestion with *Eco*R1.

The examiner also mentions the need to know what promoter regions the vectors contain and the promoter regions the vectors contain and what conditions are appropriate to express the encoded polypeptides. Since the art could obtain the cDNA from the deposit, there is no need to expression clone it and therefore there is no need to know what promoter regions are in the deposited vector. In any event, the complete structure of λGT11 (the vector disclosed in the specification) was well known at the time of the parent application, so the art would be at no disability in obtaining or using the cDNA deposited in that vector.

The examiner objects that the antibodies which applicant used to obtain these cDNA are not available. The art would not need these antibodies in view of the deposit of the resulting clones described above.

The examiner objects that the art would not be able to obtain TR2B by hybridization because the sequences are not provided. The art would not need the sequences because the cDNA itself is available from the deposit.

II. Fragments; Hybridization under stringent conditions

The examiner concludes that the specification does not enable nucleic acid sequences that hybridize with the deposited cDNA under stringent conditions (language now in claim 9). The examiner objects that this claim term includes "a virtually limitless number of possible sequences" and the "specification is silent on providing even one example of a sequence or rules of guidance for a nucleic acid sequence that hybridizes to the claimed [cDNA] under low stringency conditions." In fact, however, the claim specifies high stringency hybridization, and it is far narrower in scope than the examiner's analysis implies. It is not clear from the office action exactly what information the art lacks. Clearly, the art knows how to conduct high stringency hybridization. On this issue, the Examiner is directed to enclosure B, an excerpt from the manual Current Protocols in Molecular Biology. In this excerpt, guidance is provided for determining "standard hybridization conditions" for any given DNA probe, and applicants assert that such a determination is entirely routine for those skilled in the art. Indeed, it was essentially this very approach was demonstrably successful in the rescreening reported in the specification. In short, the art has both the biological materials and the technique for hybridization to practice claim 9.

The examiner's analysis implies that the claim is not enabled unless the art knows in advance what sequences will hybridize. Of course, the art would not be so limited in

carrying out the hybridizations. The art would be able to use the deposited cDNA to locate other DNA that stringently hybridizes, and such experiments were routine in 1989. Applicant therefore does not understand the reference to low stringency quoted above or the reference to the need for DNA that would be synthesized based on known sequence information.

Finally, the examiner has objected that the term "high" stringency is vague. To further characterize the hybridizing DNA covered by the claim, applicant requires that such DNA retain the activity of the parent cDNA -- enhancing a neuronal regenerative process.

Conclusion

If there are any other charges, or any credits, please apply them to Deposit Account No. 06-1050.

Respectfully submitted,

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